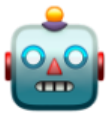

First Aid

1. Embryology

- **Heart Morphogenesis:**
  - First functional organ, beats spontaneously by week 4.
  - Cardiac looping: Week 4, establishes left-right polarity. Defect in left-right dynein → dextrocardia (Kartagener syndrome).
- **Septation of Chambers:**
  - **Atria:**
    - Septum primum grows, narrowing ostium primum.
    - Ostium secundum forms in septum primum (cell death).
    - Septum secundum develops, covers most of ostium secundum, residual foramen ovale.
    - Foramen ovale closes after birth (↑ LA pressure, ↓ RA pressure).
    - Patent foramen ovale: failure of septum primum/secundum to fuse (25% population), usually asymptomatic, can cause paradoxical emboli.
  - **Ventricles:**
    - Muscular interventricular septum forms.
    - Aorticopulmonary septum rotates/fuses with muscular septum → membranous interventricular septum, closing interventricular foramen.
    - Ventricular septal defect (VSD): most common congenital cardiac anomaly, usually in membranous septum.
  - **Outflow Tract:**

        - Neural crest cell migration → truncal/bulbar ridges spiral/fuse → aorticopulmonary septum (ascending aorta, pulmonary trunk).
        - Conotruncal abnormalities (neural crest cell migration failure): Transposition of great arteries, Tetralogy of Fallot, Persistent truncus arteriosus.
    - **Valve Development:**
        - Aortic/pulmonary: endocardial cushions of outflow tract.
        - Mitral/tricuspid: fused endocardial cushions of AV canal.
        - Anomalies: stenotic, regurgitant, atretic (tricuspid atresia), displaced (Ebstein anomaly).
- **Fetal Circulation:**
    - Umbilical vein: high O2 blood (PO2 ≈ 30 mmHg, 80% sat). Umbilical arteries: low O2.
    - **3 Important Shunts:**
        1. **Ductus venosus:** umbilical vein → IVC, bypassing hepatic circulation.
        2. **Foramen ovale:** highly oxygenated blood from IVC → LA, bypassing pulmonary circulation.
        3. **Ductus arteriosus:** deoxygenated blood from SVC → RA → RV → main pulmonary artery → ductus arteriosus → descending aorta, bypassing pulmonary circulation (due to high fetal pulmonary artery resistance).
    - **At Birth:**
        - Infant takes breath → ↓ pulmonary vascular resistance → ↑ LA pressure vs RA pressure → foramen ovale closes (fossa ovalis).
        - ↑ O2 (respiration) and ↓ prostaglandins (placental separation) → ductus arteriosus closure (ligamentum arteriosum).
        - NSAIDs (indomethacin, ibuprofen), acetaminophen: help close PDA.
        - Prostaglandins E1 and E2: KEEP PDA open.
- **Fetal-Postnatal Derivatives:**

- Ductus arteriosus → Ligamentum arteriosum (near L recurrent laryngeal nerve).
- Ductus venosus → Ligamentum venosum.
- Foramen ovale → Fossa ovalis.
- Allantois urachus → Median umbilical ligament.
- Umbilical arteries → Medial umbilical ligaments.
- Umbilical vein → Ligamentum teres hepatis (round ligament, in falciform ligament).

2. Anatomy

- **Heart Anatomy:**
  - **LA:** Most posterior part. Enlargement (mitral stenosis) → dysphagia (esophagus compression), hoarseness (L recurrent laryngeal nerve compression - Ortner syndrome).
  - **RV:** Most anterior part, most commonly injured in trauma.
  - **LV:** About 2/3 of inferior cardiac surface.
- **Pericardium:**
  - 3 layers (outer to inner): Fibrous, Parietal, Epicardium (visceral pericardium).
  - Pericardial space: between parietal pericardium and epicardium.
  - Innervated by phrenic nerve. Pericarditis → referred pain to neck, arms, shoulders.
- **Coronary Blood Supply:**
  - **LAD:** Anterior 2/3 interventricular septum, anterolateral papillary muscle, anterior LV. Most commonly occluded.
  - **PDA:** Posterior 1/3 interventricular septum, posterior 2/3 ventricular walls, posteromedial papillary muscle.
  - **RCA:** SA node, AV node. Infarct → nodal dysfunction (bradycardia, heart block). Right (acute) marginal artery supplies RV.

- **Dominance:**
  - Right-dominant (most common): PDA from RCA.
  - Left-dominant: PDA from LCX.
  - Codominant: PDA from both LCX and RCA.
- Coronary blood flow to LV/interventricular septum peaks in early diastole.
- **Coronary sinus:** Runs in L AV groove, drains into RA.

- **Cardiac Catheterization:**
  - **Pulmonary artery catheter (Swan-Ganz):** Measures R-sided pressures, PCWP (approximates LAP).
  - **Trans-septal Left Atrial Catheterization:** Direct LAP measurement, ablation.

3. Physiology

- **Cardiac Output (CO) Variables:**
  - **Stroke Volume (SV):** EDV - ESV. Affected by Contractility, Afterload, Preload (SV CAP).
    - ↑ SV with: ↑ Contractility, ↑ Preload, ↓ Afterload.
  - **Contractility (and SV):**
    - ↑ with: Catecholamine stimulation (β1 → PKA → ↑ Ca2+ ATPase, ↑ Ca2+ entry, ↑ Ca2+-induced Ca2+ release), ↑ intracellular Ca2+, Digoxin (blocks Na+/K+ pump → ↑ intracellular Na+ → ↓ Na+/Ca2+ exchanger → ↑ intracellular Ca2+).
    - ↓ with: β-blockade, HF (systolic dysfunction), acidosis, hypoxia/hypercapnia, nondihydropyridine Ca2+ channel blockers.
  - **Preload:** Approximated by EDV. Depends on venous tone, circulating blood volume. Venous vasodilators (nitroglycerin) ↓ preload.
  - **Afterload:** Approximated by MAP. Depends on wall tension (Laplace's law: Wall tension = (pressure x radius) / (2 x wall thickness)). Arterial vasodilators (hydralazine) ↓ afterload. ACE inhibitors/ARBs ↓ both preload and afterload.

- **Heart Rate (HR):** CO = SV x HR. Tachycardia → ↓ diastole time → ↓ myocardial perfusion, ↓ diastolic filling → ↓ SV → ↓ CO.
- **Myocardial O2 Demand:** ↑ with: ↑ contractility, ↑ afterload, ↑ HR, ↑ diameter of ventricle.

- **Cardiac Output Equations:**
  - SV = EDV - ESV
  - EF = SV / EDV (Normal 50-70%). Index of ventricular contractility (↓ in systolic HF, normal in diastolic HF).
  - CO = SV x HR.
  - Fick Principle: CO = (Rate of O2 consumption) / (Arterial O2 content - Venous O2 content).
  - **Pulse Pressure (PP):** SBP - DBP. Directly proportional to SV, inversely proportional to arterial compliance.
    - ↑ PP in: AR, aortic stiffening (isolated systolic HTN), OSA, high-output state, exercise.
    - ↓ PP in: AS, cardiogenic shock, cardiac tamponade, advanced HF.
  - **Mean Arterial Pressure (MAP):** CO x TPR. Also 2/3 DBP + 1/3 SBP.
- **Starling Curves:**
  - Force of contraction proportional to end-diastolic length (preload).
  - ↑ contractility with catecholamines, positive inotropes. ↓ contractility with MI, β-blockers, nondihydropyridine Ca2+ channel blockers, HF.
- **Cardiac and Vascular Function Curves:**
  - Intersection = operating point (venous return = CO).
  - **↑ Inotropy:** CF curve shifts up/left.
  - **↓ Inotropy:** CF curve shifts down/right.
  - **↑ Volume/Venous Tone:** VR curve shifts right.
  - **↓ Volume/Venous Tone:** VR curve shifts left.
  - **↑ TPR:** VR curve shifts down/right.

- **↓ TPR:** VR curve shifts up/left.

- **Resistance, Pressure, Flow:**
  - Flow (Q) = (ΔP r^4) / (8 η l). (Poiseuille's Law).
  - Resistance (R) ∝ (η l) / r^4.
  - Capillaries: highest total cross-sectional area, lowest flow velocity.
  - Arterioles: most of TPR. Veins: most blood storage.
  - Viscosity: ↑ in hyperproteinemic states, polycythemia; ↓ in anemia.
- **Pressure-Volume Loops:**
  - **Key Principles:**
    - Valves closed during isovolumetric phases (vertical lines).
    - Width of loop ≈ SV.
    - Area of loop ≈ Ventricular Stroke Work.
    - Ventricular compliance forms base of loop.
  - **Phases (LV):**
    1. Isovolumetric contraction: Mitral valve closes (S1) → aortic valve opens. Highest O2 consumption.
    2. Systolic ejection: Aortic valve opens → aortic valve closes.
    3. Isovolumetric relaxation: Aortic valve closes (S2) → mitral valve opens.
    4. Rapid filling: Just after mitral valve opening (S3).
    5. Reduced filling: Just before mitral valve closing (S4).
  - **Determinants:**
    - ↑ Preload → EDV shifts right.
    - ↑ Contractility → ESV shifts left.
    - ↑ Afterload → ESV shifts right, ↑ LVP during isovolumetric contraction.
  - **Valvular Disease Effects:**
    - **AS:** ↑ Afterload, ↓ SV. Concentric hypertrophy.

        - **AR:** ↑ Preload, ↑ SV. Loss of isovolumetric phases. Loss of dicrotic notch.
        - **MS:** ↓ Preload, ↓ SV. LA pressure >> LV pressure during diastole.
        - **MR:** ↑ Preload, ↑ SV (total). Loss of isovolumetric phases. Tall V-wave.
- **Heart Sounds:**
    - **S1:** Mitral/tricuspid valve closure. Loudest at mitral area.
    - **S2:** Aortic (A2) and pulmonary (P2) valve closure. Loudest at L upper sternal border.
        - **Physiologic Splitting:** Narrows in expiration, widens in inspiration (delayed P2).
        - **Wide Splitting:** Delayed RV emptying (pulmonic stenosis, RBBB). Exaggeration of normal.
        - **Fixed Splitting:** ASD (L-R shunt → ↑ RA/RV volumes → delayed P2, independent of respiration).
        - **Paradoxical Splitting:** Delayed aortic valve closure (AS, LBBB). P2 before A2. Split eliminated on inspiration.
    - **S3:** Early diastole, rapid ventricular filling. "Gallop." Physiologic (children, young adults, athletes, pregnancy). Pathologic (systolic HF, MR, AR, thyrotoxicosis).
    - **S4:** Late diastole ("atrial kick"). Blood entering stiffened LV. Pathologic (diastolic HF, hypertrophy, AS). Abnormal if palpable.
- **Jugular Venous Pulse (JVP):**
    - **a wave:** Atrial contraction. Absent in AFib. "Cannon a wave" in AV dissociation.
    - **c wave:** RV contraction (tricuspid valve bulging into atrium).
    - **x descent:** Atrial relaxation, downward displacement of tricuspid valve. Reduced/absent in TR, right HF.

- **v wave:** RA pressure due to ↑ volume against closed tricuspid valve. ↑ in TR/MR.
- **y descent:** RA emptying into RV. Prominent in constrictive pericarditis. Absent in cardiac tamponade.

- **Auscultation of the Heart (APTM):**
  - **Aortic (R 2nd ICS):** AS, Flow murmur, Aortic valve sclerosis.
  - **Pulmonic (L 2nd ICS):** Pulmonic stenosis, ASD, Flow murmur.
  - **Mitral (Apex, L 5th ICS MCL):** MR, MVP, MS.
  - **Tricuspid (L 4th ICS LSB):** TR, VSD, Tricuspid stenosis.
  - **Left Sternal Border:** HOCM, AR, Pulmonic Regurgitation.
- **Maneuvers:**
  - **Standing, Valsalva (strain):** ↓ Preload → ↓ LV volume. ↑ MVP (earlier click), ↑ HCM. ↓ Most other murmurs.
  - **Passive Leg Raise, Squatting:** ↑ Preload → ↑ LV volume. ↑ Most murmurs. ↓ MVP (later click), ↓ HCM.
  - **Hand Grip:** ↑ Afterload. ↑ AR, MR, VSD. ↓ AS, HCM.
  - **Inspiration:** ↑ Venous return to R heart, ↓ venous return to L heart. ↑ Most R-sided murmurs. ↓ Most L-sided murmurs.
- **Myocardial Action Potential (Non-Pacemaker):**
  - **Phase 0 (Upstroke):** Voltage-gated Na+ channels open (rapid depolarization).
  - **Phase 1 (Initial Repolarization):** Na+ channels inactivate, K+ channels open.
  - **Phase 2 (Plateau):** Ca2+ influx (L-type Ca2+ channels) balances K+ efflux. Ca2+ influx triggers Ca2+ release from SR (excitation-contraction coupling).
  - **Phase 3 (Rapid Repolarization):** Massive K+ efflux (slow delayed-rectifier K+ channels), Ca2+ channels close.

    - **Phase 4 (Resting Potential):** High K+ permeability.
    - Differs from skeletal muscle: plateau (Ca2+ influx), Ca2+ influx from ECF needed for Ca2+-induced Ca2+ release, gap junctions.
- **Pacemaker Action Potential (SA/AV Nodes):**
    - **Phase 0 (Upstroke):** Voltage-gated Ca2+ channels open (L-type). Fast Na+ channels permanently inactivated. Slow conduction velocity.
    - **Phases 1 & 2:** Absent.
    - **Phase 3 (Repolarization):** Ca2+ channels inactivate, ↑ K+ efflux.
    - **Phase 4 (Slow Diastolic Depolarization):** If ("funny current," slow mixed Na+/K+ current). Accounts for automaticity. Slope of phase 4 determines HR. ACh/adenosine ↓ slope, catecholamines ↑ slope.
- **Electrocardiogram (ECG):**
    - **Conduction Pathway:** SA node → atria → AV node → Bundle of His → R/L bundle branches → Purkinje fibers → ventricles.
    - **SA Node:** Pacemaker, near SVC opening.
    - **AV Node:** Interatrial septum, near coronary sinus. 100-msec delay (ventricular filling). Blood supply usually from RCA.
    - **Speed of Conduction:** His-Purkinje > Atria > Ventricles > AV node ("He Parks At Ventura AVenue").
    - **Waves/Intervals:**
        - **P wave:** Atrial depolarization.
        - **PR interval:** Start of atrial to start of ventricular depolarization (120-200 msec normal).
        - **QRS complex:** Ventricular depolarization (<100 msec normal).
        - **QT interval:** Ventricular depolarization, contraction, repolarization.
        - **T wave:** Ventricular repolarization. Inversion → ischemia/recent MI.
        - **J point:** End of QRS, start of ST segment.
        - **ST segment:** Isoelectric, ventricles depolarized.

        - **U wave:** Prominent in hypokalemia, bradycardia.
- **Baroreceptors and Chemoreceptors:**
    - **Baroreceptors:**
        - Aortic arch (vagus nerve), Carotid sinus (glossopharyngeal nerve). Respond to BP changes.
        - Hypotension → ↓ stretch → ↓ afferent firing → ↑ sympathetic, ↓ parasympathetic → vasoconstriction, ↑ HR, ↑ contractility, ↑ BP.
        - Carotid massage → ↑ carotid sinus pressure → ↑ afferent firing → ↑ AV node refractory period → ↓ HR, ↓ CO, peripheral vasodilation.
        - Cushing reflex: ↑ ICP → cerebral ischemia → ↑ pCO_2, ↓ pH → central sympathetic ↑ → hypertension → baroreceptor-induced bradycardia.
    - **Chemoreceptors:**
        - Peripheral (carotid/aortic bodies): Stimulated by ↓ PO_2, ↓ pH, ↑ PCO_2.
        - Central: Stimulated by pH/PCO_2 changes in brain interstitial fluid. Less responsive with chronic ↑ PCO_2.
- **Normal Resting Cardiac Pressures:**
    - RA: <5 mmHg
    - RV: 25/<5 mmHg
    - PA: 25/8 mmHg
    - PCWP: 4-12 mmHg (approximates LAP, except in MS).
    - LV: 120/<12 mmHg
    - Aorta: 120/80 mmHg
- **Autoregulation:** Blood flow to organ constant over wide range of perfusion pressures.
    - Lungs: Hypoxia → vasoconstriction.
    - Heart: Local metabolites (NO, CO_2, ↓ O_2).
    - Brain: Local metabolites (CO_2/pH).

- Kidneys: Myogenic, tubuloglomerular feedback.
- Skeletal muscle: Local metabolites during exercise (CO_2, H^+, Adenosine, Lactate, K^+).
- Skin: Sympathetic vasoconstriction (temperature control).

- **Capillary Fluid Exchange (Starling Forces):**
  - $J_v = K_f [(P_c - P_i) - \sigma (\pi_c - \pi_i)]$
  - P_c: capillary hydrostatic pressure (pushes out).
  - P_i: interstitial hydrostatic pressure (pushes in).
  - π_c: plasma oncotic pressure (pulls in).
  - π_i: interstitial fluid oncotic pressure (pulls out).
  - Edema causes: ↑ P_c, ↑ K_f, ↑ π_i, ↓ π_c.
- **Natriuretic Peptides (ANP, BNP):**
  - **ANP:** From atrial myocytes, response to ↑ blood volume/atrial pressure. Via cGMP. Vasodilation, ↓ Na^+ reabsorption (renal collecting tubule).
  - **BNP:** From ventricular myocytes, response to ↑ tension. Similar to ANP, longer half-life. Used for diagnosing HF.

4. Pathology

- **Congenital Heart Diseases:**
  - **Right-to-Left Shunts ("Blue Babies"):** Early cyanosis. Require urgent surgery/PDA maintenance. The 5 T's:
    1. **Truncus Arteriosus:** Fails to divide into PA/aorta (failure of aorticopulmonary septum). Accompanied VSD.
    2. **D-Transposition of Great Arteries:** Aorta leaves RV, PA leaves LV (failure of aorticopulmonary septum to spiral). Not compatible with life without shunt (VSD, PDA, PFO). "Egg on a string" CXR.
    3. **Tricuspid Atresia:** Absence of tricuspid valve, hypoplastic RV. Requires ASD and VSD/PDA for viability. ECG: RA hypertrophy, LV hypertrophy.

4. **Tetralogy of Fallot:** Anterosuperior displacement of infundibular septum. Most common cause of early childhood cyanosis. PROVe:
    - **P**ulmonary infundibular **S**tenosis (most important determinant for prognosis).
    - **R**VH (boot-shaped heart CXR).
    - **O**verriding aorta (straddles VSD).
    - **V**SD.
    - Pulmonary stenosis forces R-L flow across VSD → "tet spells" (crying, fever, exercise). Squatting ↓ R-L shunt. Assoc: 22q11 syndromes.
5. **Total Anomalous Pulmonary Venous Return (TAPVR):** Pulmonary veins drain into R heart circulation. Assoc: ASD, sometimes PDA.

- **Ebstein Anomaly:** Displacement of tricuspid valve leaflets into RV. Assoc: TR, accessory conduction pathways, R-sided HF. Lithium exposure in utero.
- **Left-to-Right Shunts (Acyanotic then "Later" Cyanosis):** VSD > ASD > PDA.
    1. **Ventricular Septal Defect (VSD):** Asymptomatic at birth, may manifest weeks later. Smaller defects self-resolve. Larger defects → ↑ pulmonary blood flow, LV overload, HF. O2 saturation ↑ in RV and PA.
    2. **Atrial Septal Defect (ASD):** Defect in interatrial septum. Systolic ejection murmur with wide, fixed split S2. Ostium secundum most common. Can lead to paradoxical emboli. Assoc: Down syndrome. O2 saturation ↑ in RA, RV, PA.
    3. **Patent Ductus Arteriosus (PDA):** Continuous "machinelike" murmur (L infraclavicular area, loudest S2). Maintained by PGE synthesis, low O2 tension. Uncorrected → late cyanosis in lower extremities (differential cyanosis). Assoc: Congenital rubella, prematurity.
- **Eisenmenger Syndrome:** Uncorrected L-R shunt → ↑ pulmonary blood flow → pulmonary arterial hypertension → RVH → shunt becomes R-L. Causes late cyanosis, clubbing, polycythemia.

- **Coarctation of the Aorta:** Aortic narrowing near ductus arteriosus ("juxtaductal"). Assoc: Bicuspid AV, Turner syndrome. HTN in upper extremities, cold/weak/delayed pulses in lower (brachiofemoral delay). CXR: rib notching (collateral circulation). Complications: HF, cerebral hemorrhage (berry aneurysms), aortic rupture, IE.
- **Persistent Pulmonary Hypertension of Newborn:** Persistence of ↑ pulmonary vascular resistance after birth. R-L shunt through PFO/PDA. Respiratory distress, cyanosis. Preductal O_2 sat > postductal.

- **Congenital Cardiac Defect Associations:**
  - Prenatal alcohol: VSD, PDA, ASD, ToF.
  - Congenital rubella: PDA, pulmonary artery stenosis, septal defects.
  - Down syndrome: AV septal defect, VSD, ASD.
  - Infant of diabetic mother: Transposition, truncus arteriosus, tricuspid atresia, VSD.
  - Marfan syndrome: MVP, thoracic aortic aneurysm/dissection, AR.
  - Prenatal lithium: Ebstein anomaly.
  - Turner syndrome: Bicuspid AV, coarctation.
  - Williams syndrome: Supravalvular aortic stenosis.
  - 22q11 syndromes: Truncus arteriosus, ToF.
- **Hypertension:**
  - **Overview:** SBP ≥130 mmHg and/or DBP ≥80 mmHg. 90% essential (1°), 10% secondary.
  - **Risk Factors:** Age, obesity, diabetes, inactivity, high-Na diet, alcohol, tobacco, family history.
  - **Secondary HTN Causes:** Renal/renovascular (fibromuscular dysplasia "string of beads," atherosclerotic renal artery stenosis), 1° hyperaldosteronism, OSA, Cushing syndrome, pheochromocytoma, hyperthyroidism.
  - **Hypertensive Urgency:** ≥180/120 mmHg, no end-organ damage.

    - **Hypertensive Emergency:** ≥180/120 mmHg + acute end-organ damage (encephalopathy, stroke, retinal hemorrhages, papilledema, MI, HF, aortic dissection, kidney injury, microangiopathic hemolytic anemia, eclampsia). Arterioles: fibrinoid necrosis.
    - **Predisposes to:** CAD, LVH, HF, AFib, aortic dissection/aneurysm, stroke, CKD, retinopathy.
- **Hyperlipidemia Signs:**
    - **Xanthomas:** Lipid-laden histiocytes in skin (xanthelasma on eyelids).
    - **Tendinous Xanthoma:** Lipid deposit in Achilles tendon/finger extensors. Assoc: familial hypercholesterolemia.
    - **Corneal Arcus:** Lipid deposit in cornea. Common in elderly (arcus senilis), earlier with hypercholesterolemia.
- **Atherosclerosis:**
    - **Location:** Abdominal aorta > coronary artery > popliteal artery > carotid artery > circle of Willis.
    - **Risk Factors:** Modiable (HTN, smoking, dyslipidemia, diabetes), Non-modiable (age, male, postmenopausal, family history).
    - **Progression:** Endothelial dysfunction → macrophage/LDL accumulation → foam cells → fatty streaks → smooth muscle cell migration/proliferation/ECM deposition → fibrous plaque → complex atheromas → calcification. Inflammation is key.
    - **Complications:** Ischemia, infarction, aneurysm, PVD, thrombosis, embolism.
- **Cholesterol Emboli Syndrome:** Microembolization of cholesterol from atherosclerotic plaques (aorta). End-organ damage (livedo reticularis, blue toe, AKI, CVA, gut ischemia). Pulses palpable. Follows vascular procedures.
- **Arteriolosclerosis:** Affects small arteries/arterioles.
    - **Hyaline:** Vessel wall thickening (plasma protein leak) in HTN/diabetes.
    - **Hyperplastic:** "Onion skinning" (smooth muscle proliferation) in severe HTN.

- **Aortic Aneurysm:** Localized dilation. Abdominal/back pain → leaking/dissection/rupture.
    - **Thoracic:** Assoc: cystic medial degeneration, HTN, bicuspid AV, CTD, 3° syphilis (vasa vasorum endarteritis). Aortic root dilation → AR/dissection. "Tree bark" aorta (syphilis).
    - **Abdominal:** Assoc: transmural inflammation, ECM degradation. Risk: smoking (strongest), age, male, family history. Pulsatile abdominal mass. Rupture triad: pulsatile abdominal mass, acute abdominal/back pain, resistant hypotension. Most infrarenal.
- **Traumatic Aortic Rupture:** Trauma/deceleration injury. Most common at aortic isthmus (just distal to L subclavian). Widened mediastinum CXR.
- **Aortic Dissection:** Longitudinal intimal tear → false lumen.
    - **Assoc:** HTN (strongest), bicuspid AV, CTD (Marfan).
    - **Presentation:** Tearing, sudden-onset chest pain radiating to back. Unequal BP in arms. Widened mediastinum CXR.
    - **Complications:** Organ ischemia, aortic rupture, death.
    - **Stanford Classification:**
        - **Type A (Proximal):** Involves ascending aorta. Acute AR, cardiac tamponade. Treatment: surgery.
        - **Type B (Distal):** Only descending aorta (below L subclavian). Treatment: β-blockers, then vasodilators.
- **Subclavian Steal Syndrome:** Stenosis of subclavian artery (proximal to vertebral artery origin) → hypoperfusion distal to stenosis → reversed blood flow in ipsilateral vertebral artery → reduced cerebral perfusion on arm exertion. Arm ischemia, pain, paresthesia, vertebrobasilar insufficiency. >15 mmHg BP difference between arms. Assoc: atherosclerosis, Takayasu arteritis, heart surgery.
- **Coronary Artery Disease (CAD):**
    - **Angina:** Chest pain due to ischemic myocardium (no necrosis).

        - **Stable:** Atherosclerosis (>70% occlusion). Exertional pain, resolves with rest/nitroglycerin.
        - **Unstable:** Thrombosis with incomplete occlusion. ↑ frequency/intensity, or at rest. No cardiac biomarker elevation.
        - **Vasospastic (Prinzmetal/Variant):** At rest, coronary artery spasm. Transient ischemic ST changes. Risk: smoking. Triggers: cocaine, amphetamines, alcohol, triptans. Treat: Ca2+ channel blockers, nitrates, smoking cessation.
    - **Myocardial Infarction (MI):** Rupture of atherosclerotic plaque → acute thrombosis. ↑ cardiac biomarkers (CK-MB, troponins).
        - **NSTEMI:** Subendocardial infarct. ST depression, T-wave inversion. Elevated troponins.
        - **STEMI:** Transmural infarct. ST elevation, pathologic Q waves. Elevated troponins.
    - **Coronary Steal Syndrome:** Distal to stenosis, vessels maximally dilated. Vasodilators (dipyridamole, regadenoson) dilate normal vessels → blood shunted to well-perfused areas → ischemia in stenosed areas.
    - **Sudden Cardiac Death (SCD):** Unexpected death within 1 hour of symptom onset. Most commonly lethal arrhythmia (VFib). Assoc: CAD, cardiomyopathy, channelopathies. Prevent: ICD.
    - **Chronic Ischemic Heart Disease:** Progressive HF over years due to chronic ischemia.
        - **Myocardial hibernation:** Reversible LV systolic dysfunction in chronic ischemia.
        - **Myocardial stunning:** Transient LV systolic dysfunction after brief acute ischemia.
- **Evolution of Myocardial Infarction:**
    - **Commonly Occluded Arteries:** LAD > RCA > circumflex.
    - **Symptoms:** Diaphoresis, nausea, vomiting, severe retrosternal pain, L arm/jaw pain, SOB, fatigue.

- **Timeframe / Gross / Light Microscope / Complications:**
  - **0-24 hours:** Dark mottling; wavy fibers (0-4hr), early coagulative necrosis (4-24hr), edema, hemorrhage. Reperfusion injury (dark eosinophilic stripes). Complications: Ventricular arrhythmia, HF, cardiogenic shock.
  - **1-3 days:** Hyperemia; extensive coagulative necrosis, acute inflammation with neutrophils. Complication: Postinfarction fibrinous pericarditis.
  - **3-14 days:** Hyperemic border, central yellow-brown softening; macrophages, then granulation tissue at margins. Complications: Free wall rupture → tamponade; papillary muscle rupture → acute MR; interventricular septal rupture (VSD) → L-R shunt; LV pseudoaneurysm (risk of rupture).
  - **2 weeks-months:** Gray-white scar; contracted scar complete. Complications: Postcardiac injury syndrome (Dressler), HF, arrhythmias, true ventricular aneurysm (risk of mural thrombus).

- **Diagnosis of MI:**
  - First 6 hours: ECG gold standard.
  - **Cardiac Troponin I:** Rises after 4 hours (peaks 24hr), ↑ for 7-10 days. More specific.
  - **CK-MB:** Increases after 6-12 hours (peaks 16-24hr), normal after 48 hours. Useful for reinfarction.
  - **ECG Changes:** ST elevation (STEMI), ST depression (NSTEMI), hyperacute T waves, T-wave inversion, pathologic Q waves, poor R wave progression.
  - **ECG Localization of STEMI:**
    - Anteroseptal (LAD): V1-V2
    - Anteroapical (distal LAD): V3-V4
    - Anterolateral (LAD or LCX): V5-V6
    - Lateral (LCX): I, aVL
    - Inferior (RCA): II, III, aVF

        - Posterior (PDA): V7-V9, ST depression in V1-V3 with tall R waves.
- **Narrow Complex Tachycardias (<120 msec QRS):** Originates within or above AV node.
    - **Atrial Fibrillation (AFib):** Irregularly irregular, no discrete P waves. Foci near pulmonary vein ostia. Risk: HTN, CAD. Complications: thromboembolism (stroke). Mgmt: rate/rhythm control, cardioversion, ablation (pulmonary vein ostia).
    - **Multifocal Atrial Tachycardia:** Irregularly irregular, ≥3 distinct P wave morphologies. Assoc: COPD, pneumonia, HF.
    - **Atrial Flutter:** Rapid identical "sawtooth" P waves. Reentry circuit around tricuspid annulus (R atrium). Mgmt: like AFib, ablation.
    - **Paroxysmal Supraventricular Tachycardia (PSVT):** Reentrant tract (most common AV node). Sudden-onset palpitations. ECG: narrow QRS tachycardia, HR >150, P wave buried. Mgmt: vagal maneuvers, adenosine, CCBs, β-blockers. Unstable: electrical cardioversion. Ablation.
    - **Wolff-Parkinson-White (WPW) Syndrome:** Accessory pathway (Bundle of Kent) bypasses AV node.
        - ECG: Short PR, delta wave, wide QRS.
        - Can result in reentry circuit → SVT.
        - Mgmt: Procainamide, ibutilide. Avoid AV nodal-blocking drugs (adenosine, CCBs, β-blockers).
- **Wide Complex Tachycardias (≥120 msec QRS):** Originates below AV node.
    - **Ventricular Tachycardia (VT):** Regular rhythm, rate >100. Structural heart disease (MI scarring). High risk SCD.
    - **Torsades de Pointes (TdP):** Polymorphic VT, shifting sinusoidal waveforms. Prolonged QT interval predisposes. Causes: drugs (ABCDEF+NO), ↓ K+, ↓ Mg2+, ↓ Ca2+. Mgmt: defibrillation (unstable), MgSO4 (stable).
    - **Ventricular Fibrillation (VFib):** Disorganized rhythm, no identifiable waves. Fatal without immediate CPR/defibrillation.

- **Hereditary Channelopathies:** Inherited mutations of cardiac ion channels → abnormal AP → ↑ risk VT/SCD.
    - **Brugada Syndrome:** AD, Na+ channel loss-of-function. Asian males. Pseudo-RBBB, ST-elevation V1-V2. Prevent SCD with ICD.
    - **Congenital Long QT Syndrome:** K+ channel loss-of-function (repolarization affected).
        - **Romano-Ward:** AD, pure cardiac (no deafness).
        - **Jervell and Lange-Nielsen:** AR, sensorineural deafness.
- **Sick Sinus Syndrome:** Age-related SA node degeneration. Bradycardia, sinus pauses/arrest, junctional escape beats. Tachycardia-bradycardia syndrome.
- **Conduction Blocks:**
    - **First-degree AV block:** PR interval >200 msec. Benign.
    - **Second-degree AV block:**
        - **Mobitz Type I (Wenckebach):** Progressive PR lengthening until QRS dropped. Regularly irregular. Benign.
        - **Mobitz Type II:** Intermittent non-conducted P waves (dropped QRS), no PR lengthening. High risk → pacemaker.
    - **Third-degree (Complete) AV block:** P waves and QRS dissociated. Atrial rate > ventricular rate. Assoc: Lyme disease. High risk → pacemaker.
    - **Bundle Branch Block:** Interruption of conduction in L/R bundle branches. Affected ventricle depolarizes via slower myocyte-to-myocyte conduction.
        - **RBBB:** "M" shape V1, slurring S-wave V6.
        - **LBBB:** No R waves V1, notched R waves V6.
- **Premature Beats:**
    - **Premature Atrial Contraction (PAC):** Ectopic foci in atria. Narrow QRS, preceding P wave. Benign, but ↑ AFib/flutter risk.
    - **Premature Ventricular Contraction (PVC):** Ectopic beats from ventricle. Wide QRS, no preceding P wave.

- **Myocardial Infarction Complications (Timeframe, Findings, Notes):**
  - **Cardiac arrhythmia:** First few days to months. Myocardial death/scarring.
  - **Peri-infarction pericarditis:** 1-3 days. Pleuritic chest pain, friction rub, ECG changes. Self-limited.
  - **Papillary muscle rupture:** 2-7 days. Acute MR → cardiogenic shock, pulmonary edema. Posteromedial (single PDA supply) > anterolateral.
  - **Interventricular septal rupture:** 3-5 days. VSD → ↑ O2 sat/pressure in RV.
  - **Ventricular pseudoaneurysm:** 3-14 days. Free wall rupture contained by pericardium/scar. Does not contain endocardium/myocardium. High rupture risk.
  - **Ventricular free wall rupture:** 5-14 days. Cardiac tamponade. Acute form → sudden death. LVH/previous MI protect.
  - **True ventricular aneurysm:** 2 weeks-months. Outward bulge with contraction ("dyskinesia"). Assoc: fibrosis.
  - **Postcardiac injury syndrome (Dressler syndrome):** Weeks-months. Fibrinous pericarditis (autoimmune).
- **Cardiomyopathies:**
  - **Dilated Cardiomyopathy (Systolic Dysfunction):** Most common (90%). Eccentric hypertrophy (sarcomeres in series) → ↑ LV mass, ↑ LV cavity, ↓ EF.
    - **Causes:** Idiopathic/familial (TTN gene), drugs (alcohol, cocaine, doxorubicin), infection (coxsackie B, Chagas), ischemia, systemic (hemochromatosis, sarcoidosis, thyrotoxicosis, wet beriberi), peripartum, Takotsubo.
    - **Findings:** HF, S3, systolic regurgitant murmur, dilated heart.
  - **Hypertrophic Cardiomyopathy (Diastolic Dysfunction):** 60-70% familial (AD, sarcomere mutations). Concentric hypertrophy (sarcomeres in parallel), often septal predominance. Myofibrillar disarray, fibrosis.
    - **HOCM:** Dynamic LV outflow tract obstruction (asymmetric septal hypertrophy, systolic anterior motion of mitral valve).

        - **Classic:** Syncope during exercise, sudden death (young athletes). Systolic crescendo-decrescendo murmur at LLSB (↑ with Valsalva, ↓ with passive leg raise). S4. Functional MR.
        - **Mgmt:** Avoid dehydration/strenuous exercise, β-blockers, nondihydropyridine CCBs. ICD if high risk. Avoid drugs that ↓ preload.
    - **Restrictive/Infiltrative Cardiomyopathy (Diastolic Dysfunction):** Stiffened ventricular walls. Normal LV mass/cavity/EF.
        - **Causes:** Postradiation fibrosis, Löeffler endocarditis (hypereosinophilic), Endocardial fibroelastosis, Amyloidosis, Sarcoidosis, Hemochromatosis (PLEASe Help!).
        - Low-voltage ECG despite thick myocardium (amyloidosis).
- **Heart Failure (HF):** Cardiac pump dysfunction → congestion, low perfusion. Dyspnea, orthopnea, fatigue, S3, rales, JVD, pitting edema.
    - **Systolic (HFrEF):** Reduced EF, ↑ EDV. ↓ Contractility. Eccentric hypertrophy.
    - **Diastolic (HFpEF):** Preserved EF, normal EDV. ↓ Compliance (↑ EDP). Concentric hypertrophy.
    - **Right HF:** Most often from Left HF. Cor pulmonale = isolated Right HF due to pulmonary cause.
    - **Left HF Symptoms:** Orthopnea, PND, pulmonary edema ("HF cells" - hemosiderin-laden macrophages).
    - **Right HF Symptoms:** Congestive hepatomegaly ("nutmeg liver"), JVD, peripheral edema.
    - **High-Output HF:** Uncommon. ↑ CO due to ↓ SVR (vasodilation/AV shunting). Causes: severe obesity, advanced cirrhosis, severe anemia, hyperthyroidism, wet beriberi, Paget disease.
    - **Mgmt (HFrEF):** ACE inhibitors/ARBs, ARNI, β-blockers (compensated), aldosterone antagonists (all ↓ mortality). Diuretics (symptomatic relief). Hydralazine + nitrate, SGLT2 inhibitors.
- **Shock:** Inadequate organ perfusion → ↑ lactic acidosis.

- **Hypovolemic:** ↓ Circulating volume. Cold, clammy. ↓ CVP, ↓ PCWP, ↓ CO, ↑ HR, ↑ SVR, ↓ SVO2.
- **Cardiogenic:** LV failure (↓ contractility). Cold, clammy. ↑ CVP, ↑ PCWP, ↓ CO, ↑ HR, ↑ SVR, ↓ SVO2.
- **Obstructive:** Impeded cardiopulmonary blood flow. Cold, clammy. ↑ CVP, ↑/↓ PCWP, ↓ CO, ↑ HR, ↑ SVR, ↓ SVO2.
- **Cardiac Tamponade:** Compression by fluid → ↓ CO. Beck's Triad (hypotension, ↑ JVP, muffled heart sounds). Pulsus paradoxus. Electrical alternans, low-voltage QRS. Dx: Echo. Mgmt: Pericardiocentesis.
- **Distributive (Septic, Anaphylactic, Neurogenic):** Systemic vasodilation (↓ SVR). Warm, dry (early) → cold, clammy (late).
  - **Septic:** ↓ CVP, ↓ PCWP, ↑ CO (early), ↑ HR, ↓ SVR, ↑ SVO2.
  - **Anaphylactic:** ↓ CVP, ↓ PCWP, ↑ CO (early), ↑ HR, ↓ SVR, ↑ SVO2.
  - **Neurogenic:** ↓ CVP, ↓ PCWP, ↓ CO, ↓ HR, ↓ SVR, normal/↑ SVO2.

- **Syncope:** Transient loss of consciousness from ↓ cerebral blood flow.
  - **Reflex (Vasovagal):** Common faint, situational (coughing, defecation, etc.), carotid sinus hypersensitivity.
  - **Orthostatic:** Hypovolemia, drugs, autonomic dysfunction. Drop in SBP >20 mmHg and/or DBP >10 mmHg on standing.
  - **Cardiac:** Arrhythmias, structural (AS, HCM).
- **Infective Endocarditis (IE):** Infection of endocardial surface (heart valves). Bacteria >> fungi.
  - **Acute:** *S. aureus* (high virulence). Large, destructive vegetations on normal valves. Rapid onset.
  - **Subacute:** Viridans streptococci (low virulence). Smaller vegetations on abnormal/diseased valves. Sequela of dental procedures. Gradual onset.
  - **Presentation:** Fever, new murmur, vascular/immunologic phenomena.
  - **Vascular Phenomena:** Septic embolism, petechiae, splinter hemorrhages, Janeway lesions (painless on palms/soles).

- **Immunologic Phenomena:** Immune complex deposition, glomerulonephritis, Osler nodes (painful on finger/toe pads), Roth spots (retinal hemorrhages with pale centers).
- **Valve Involvement:** Mitral > aortic >> tricuspid. Tricuspid IE: assoc with IVDU.
- **Common Associations:**
  - Prosthetic valves: *S. epidermidis*.
  - GI/GU procedures: *Enterococcus*.
  - Colon cancer: *S. gallolyticus*.
  - Gram-negative: HACEK organisms.
  - Culture-negative: *Coxiella, Bartonella*.
  - IVDU: *S. aureus, Pseudomonas, Candida*.
- **Pathophys:** Endothelial injury → vegetations (platelets, fibrin, microbes) → valve regurgitation, septic embolism.

- **Nonbacterial Thrombotic Endocarditis (NBTE/Marantic Endocarditis):** Noninfective. Sterile, platelet-rich thrombi on mitral/aortic valve. Asymptomatic until embolism. Assoc: hypercoagulable state (advanced malignancy, SLE - Libman-Sacks endocarditis).
- **Rheumatic Fever:** Consequence of pharyngeal infection with Group A β-hemolytic streptococci. Immune-mediated (Type II HSn). Antibodies to M protein cross-react with self-antigens.
  - **Late Sequelae:** Rheumatic heart disease (mitral > aortic >> tricuspid). Early regurgitation, late stenosis.
  - **Assoc:** Aschoff bodies (granuloma with giant cells, Anitschkow cells), ↑ ASO/anti-DNase B titers.
  - **JONES Criteria (Major):** **J**oint (migratory polyarthritis), **<3** (carditis), **N**odules (subcutaneous), **E**rythema marginatum, **S**ydenham chorea.
  - **Treatment/Prophylaxis:** Penicillin.

- **Syphilitic Heart Disease:** 3° syphilis disrupts vasa vasorum of aorta → atrophy of vessel wall, dilation of aorta/valve ring. "Tree bark" appearance of aorta. Aneurysm of ascending aorta/arch, AR.
- **Acute Pericarditis:** Inflammation of pericardium.
  - **Presentation:** Sharp, pleuritic retrosternal chest pain. Improves leaning forward, worsens lying down. Friction rub.
  - **ECG:** Widespread ST-elevation, PR-depression.
  - **Etiology:** Idiopathic, viral (Coxsackievirus B), malignancy, cardiac surgery, radiotherapy, MI (postcardiac injury syndrome), autoimmune, uremia.
  - **Complications:** Pericardial effusion → tamponade, constrictive pericarditis.
- **Constrictive Pericarditis:** Chronic inflammation → pericardial fibrosis/calcification → restricted ventricular filling.
  - **Etiology:** Chronic pericarditis, radiation, TB (common in resource-limited countries).
  - **Presentation:** Dyspnea, peripheral edema, JVD, Kussmaul sign, pulsus paradoxus, pericardial knock.
- **Kussmaul Sign:** Paradoxical ↑ in JVP on inspiration. Impaired RV filling. Seen in constrictive pericarditis, restrictive cardiomyopathy, right HF, massive PE, right atrial/ventricular tumors.
- **Myocarditis:** Inflammation of myocardium. Major cause of SCD in adults <40.
  - **Presentation:** Variable: dyspnea, chest pain, fever, arrhythmias (persistent tachycardia out of proportion to fever).
  - **Causes:** Viral (Coxsackie B, adenovirus, parvovirus B19, HIV, HHV-6, COVID-19 - lymphocytic infiltrate, focal necrosis), parasitic (Trypanosoma cruzi, Toxoplasma gondii), bacterial (Borrelia burgdorferi, Mycoplasma pneumoniae, Corynebacterium diphtheriae), toxins, rheumatic fever, drugs (doxorubicin, cocaine), autoimmune.
  - **Complications:** SCD, arrhythmias, heart block, dilated cardiomyopathy, HF, mural thrombus/emboli.

- **Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu):** AD disorder of blood vessels. Blanching lesions (telangiectasias), recurrent epistaxis, AVMs (brain, lung, liver), GI bleed, hematuria.
- **Cardiac Tumors:**
    - **Metastasis:** Most common cardiac tumor (melanoma).
    - **Myxomas:** Most common 1° cardiac tumor in adults. 90% in atria (mostly LA). "Ball valve" obstruction in LA → syncope. IL-6 production → constitutional symptoms. Early diastolic "tumor plop." Histology: gelatinous material, myxoma cells in glycosaminoglycans.
    - **Rhabdomyomas:** Most frequent 1° cardiac tumor in children. Assoc: tuberous sclerosis. Hamartomatous growths. More common in ventricles.

5. Pharmacology

- **Hypertension Treatment:**
    - **Primary (Essential) HTN:** Thiazide diuretics, ACE inhibitors, ARBs, dihydropyridine Ca2+ channel blockers.
    - **HTN with HF:** Diuretics, ACE inhibitors/ARBs, β-blockers (compensated HF), aldosterone antagonists. (β-blockers cautious in decompensated, contraindicated in cardiogenic shock). ARBs + sacubitril.
    - **HTN with Diabetes Mellitus:** ACE inhibitors/ARBs (nephroprotective), Ca2+ channel blockers, β-blockers (can mask hypoglycemia).
    - **HTN in Asthma:** ARBs, Ca2+ channel blockers, thiazide diuretics, cardioselective β-blockers. Avoid nonselective β-blockers (bronchoconstriction). Avoid ACE inhibitors (cough confusion).
    - **HTN in Pregnancy:** Nifedipine, methyldopa, labetalol, hydralazine ("New moms love hugs").
- **Cardiovascular Agents and Molecular Targets:**
    - **Nitrates (Nitroglycerin, Isosorbide dinitrate/mononitrate):**
        - **Mechanism:** ↑ NO in vascular smooth muscle → ↑ cGMP → relaxation. Dilate veins >> arteries → ↓ preload.
        - **Use:** Angina, ACS, pulmonary edema.

        - **Adverse:** Reflex tachycardia (treat with β-blockers), methemoglobinemia, hypotension, flushing, headache, "Monday disease." Contraindicated in RV infarction, HCM, concurrent PDE-5 inhibitors.
    - **Calcium Channel Blockers (CCBs):** Block voltage-dependent L-type Ca2+ channels.
        - **Dihydropyridines (Amlodipine, Clevidipine, Nicardipine, Nifedipine, Nimodipine):** Act on vascular smooth muscle (arteries > veins).
            - **Use:** HTN, angina (vasospastic), Raynaud. Nimodipine for subarachnoid hemorrhage. Nicardipine, Clevidipine for hypertensive urgency/emergency.
            - **Adverse:** Peripheral edema, flushing, dizziness, gingival hyperplasia.
        - **Nondihydropyridines (Diltiazem, Verapamil):** Act on heart > vascular smooth muscle.
            - **Mechanism:** ↓ muscle contractility, ↓ conduction velocity, ↑ ERP, ↑ PR interval.
            - **Use:** HTN, angina, AFib/flutter (rate control).
            - **Adverse:** Cardiac depression, AV block, hyperprolactinemia (verapamil), constipation, gingival hyperplasia.
    - **Hydralazine:**
        - **Mechanism:** ↑ cGMP → smooth muscle relaxation. Vasodilates arterioles > veins → afterload reduction.
        - **Use:** Severe HTN (acute), HF (with nitrate). Safe in pregnancy. Coadministered with β-blocker to prevent reflex tachycardia.
        - **Adverse:** Compensatory tachycardia (contraindicated in angina/CAD), fluid retention, headache, angina, drug-induced lupus.
    - **Hypertensive Emergency Treatment:** Labetalol, Clevidipine, Fenoldopam, Nicardipine, Nitroprusside.

        - **Nitroprusside:** Short acting (arteries = veins), direct NO release. Cyanide toxicity.
        - **Fenoldopam:** Dopamine D1 receptor agonist. Coronary, peripheral, renal, splanchnic vasodilation. ↓ BP, ↑ natriuresis.
    - **Antianginal Therapy:** Reduce myocardial O2 consumption (MVO2).
        - **Nitrates:** ↓ EDV, ↓ BP, ↑ HR (reflex), ↓ ejection time, ↓ MVO2.
        - **βblockers:** No effect/↑ EDV, ↓ BP, ↓ contractility, ↓ HR, ↑ ejection time, ↓ MVO2.
        - **Nitrates + βblockers:** No effect/↓ EDV, ↓ BP, little/no effect on contractility/HR/ejection time, ↓↓ MVO2.
        - Nondihydropyridine CCBs similar to β-blockers.
    - **Ranolazine:**
        - **Mechanism:** Inhibits late inward Na+ current → ↓ diastolic wall tension, ↓ O2 consumption. No effect on HR/BP.
        - **Use:** Refractory angina.
        - **Adverse:** Constipation, dizziness, headache, nausea.
    - **Sacubitril:**
        - **Mechanism:** Neprilysin inhibitor. Prevents degradation of bradykinin, natriuretic peptides, angiotensin II, substance P → ↑ vasodilation, ↓ ECF volume.
        - **Use:** In combination with valsartan (ARB) for HFrEF.
        - **Adverse:** Hypotension, hyperkalemia, cough, dizziness. Contraindicated with ACE inhibitors (angioedema).
    - **Lipid-Lowering Agents:**
        - **Statins (Atorvastatin, Lovastatin, Pravastatin, Rosuvastatin, Simvastatin):**
            - **Effect:** ↓↓↓ LDL, ↑ HDL, ↓ TG.

- **Mechanism:** Inhibit HMG-CoA reductase → ↓ cholesterol synthesis → ↑ LDL receptor recycling → ↑ LDL catabolism. ↓ Mortality in CAD.
- **Adverse:** Hepatotoxicity, myopathy (especially with fibrates/niacin).

- **Bile Acid Resins (Cholestyramine, Colesevelam, Colestipol):**
  - **Effect:** ↓↓ LDL, slightly ↑ HDL, slightly ↑ TG.
  - **Mechanism:** Disrupt enterohepatic bile acid circulation → ↑ cholesterol to bile conversion → ↓ intrahepatic cholesterol → ↑ LDL receptor recycling.
  - **Adverse:** GI upset, ↓ absorption of other drugs/fat-soluble vitamins.
- **Ezetimibe:**
  - **Effect:** ↓↓ LDL, ↑/— HDL, ↓/— TG.
  - **Mechanism:** Prevents cholesterol absorption at small intestine brush border.
  - **Adverse:** Rare ↑ LFTs, diarrhea.
- **Fibrates (Fenofibrate, Gemfibrozil):**
  - **Effect:** ↓ LDL, ↑ HDL, ↓↓↓ TG.
  - **Mechanism:** Activate PPAR-α → upregulate LPL → ↑ TG clearance. Induce HDL synthesis.
  - **Adverse:** Myopathy (↑ risk with statins), cholesterol gallstones.
- **Niacin:**
  - **Effect:** ↓↓ LDL, ↑↑ HDL, ↓ TG.
  - **Mechanism:** Inhibits lipolysis (hormone-sensitive lipase) in adipose tissue. Reduces hepatic VLDL synthesis.
  - **Adverse:** Flushed face (prostaglandin mediated, ↓ by NSAIDs), hyperglycemia, hyperuricemia.

        - **PCSK9 Inhibitors (Alirocumab, Evolocumab):**
            - **Effect:** ↓↓↓ LDL, ↑ HDL, ↓ TG.
            - **Mechanism:** Inactivation of LDL-receptor degradation → ↑ removal of LDL from bloodstream.
            - **Adverse:** Myalgias, delirium, dementia, neurocognitive effects.
        - **Fish Oil/Marine Omega-3 Fatty Acids:**
            - **Effect:** Slightly ↑ LDL, slightly ↑ HDL, ↓ (high doses) TG.
            - **Mechanism:** Believed to ↓ FFA delivery to liver, ↓ TG-synthesizing enzymes.
            - **Adverse:** Nausea, fishlike taste.
    - **Digoxin:**
        - **Mechanism:** Direct inhibition of Na+/K+-ATPase → indirect inhibition of Na+/Ca2+ exchanger → ↑ intracellular Ca2+ → positive inotropy. Stimulates vagus nerve → ↓ HR.
        - **Use:** HF (↑ contractility), AFib (↓ AV node conduction, SA node depression).
        - **Adverse:** Cholinergic (nausea, vomiting, diarrhea), blurry yellow vision ("van Glow"), arrhythmias, atrial tachycardia with AV block. Can lead to hyperkalemia (poor prognosis).
        - **Toxicity Predisposing Factors:** Renal failure, hypokalemia, drugs that displace digoxin (verapamil, amiodarone, quinidine), ↓ clearance.
        - **Antidote:** Normalize K+, cardiac pacer, anti-digoxin Fab fragments, Mg2+.
- **Antiarrhythmics:**
    - **Class I (Na+ Channel Blockers):** Slow/block conduction (especially depolarized cells). ↓ slope of phase 0. ↑ action at faster HR (use dependence: IC > IA > IB).
        - **IA (Quinidine, Procainamide, Disopyramide):** Moderate block. ↑ AP duration, ↑ ERP, ↑ QT interval. Some K+ channel block.

        - **Use:** Atrial/ventricular arrhythmias (reentrant, ectopic SVT/VT).
        - **Adverse:** Cinchonism (quinidine), reversible SLE-like (procainamide), HF (disopyramide), thrombocytopenia, torsades.
    - **IB (Lidocaine, Mexiletine, Phenytoin):** Weak block. ↓ AP duration. Preferentially affect ischemic/depolarized Purkinje/ventricular tissue.
        - **Use:** Acute ventricular arrhythmias (post-MI), digitalis-induced arrhythmias. "IB is Best post-MI."
        - **Adverse:** CNS stimulation/depression, cardiovascular depression.
    - **IC (Flecainide, Propafenone):** Strong block. Significantly prolongs ERP in AV node/accessory bypass tracts. Minimal effect on AP duration.
        - **Use:** SVTs (AFib). Last resort in refractory VT.
        - **Adverse:** Proarrhythmic (especially post-MI, contraindicated in structural/ischemic heart disease).
- **Class II (βblockers):** Metoprolol, Propranolol, Esmolol, Atenolol, Timolol, Carvedilol.
    - **Mechanism:** ↓ SA/AV nodal activity by ↓ cAMP, ↓ Ca2+ currents. Suppress abnormal pacemakers (↓ slope of phase 4). ↑ PR interval.
    - **Use:** SVT, ventricular rate control for AFib/flutter, prevent ventricular arrhythmia post-MI.
    - **Adverse:** Impotence, COPD/asthma exacerbation, bradycardia, AV block, HF, CNS effects (sedation, sleep alterations), mask hypoglycemia. Metoprolol → dyslipidemia. Propranolol → vasospasm. Treat overdose with saline, atropine, glucagon.
- **Class III (K+ Channel Blockers):** Amiodarone, Ibutilide, Dofetilide, Sotalol (AIDS).
    - **Mechanism:** ↑ AP duration, ↑ ERP, ↑ QT interval.
    - **Use:** AFib/flutter, VT (amiodarone, sotalol).
    - **Adverse:** Torsades (sotalol, ibutilide). Amiodarone: pulmonary fibrosis, hepatotoxicity, hypo/hyperthyroidism, corneal deposits, blue/gray skin,

neurologic effects, constipation, bradycardia, heart block, HF. Check PFTs, LFTs, TFTs. Amiodarone has Class I, II, III, IV effects.

- **Class IV (Ca2+ Channel Blockers):** Diltiazem, Verapamil.
  - **Mechanism:** ↓ Conduction velocity, ↑ ERP, ↑ PR interval.
  - **Use:** Prevention of nodal arrhythmias (SVT), rate control in AFib.
  - **Adverse:** Constipation, gingival hyperplasia, flushing, edema, HF, AV block, sinus node depression.
- **Other Antiarrhythmics:**
  - **Adenosine:** ↑ K+ out of cells (hyperpolarizes) and ↓ ICa → ↓ AV node conduction. Drug of choice for diagnosing/terminating certain SVTs. Very short acting (~15 sec). Effects blunted by theophylline/caffeine. Adverse: flushing, hypotension, chest pain, impending doom, bronchospasm.
  - **Magnesium:** Effective in torsades de pointes and digoxin toxicity.
  - **Ivabradine:** Selectively inhibits "funny" Na+ channels (If) → prolongs phase IV depolarization. Use: Chronic HFrEF. Adverse: Luminous phenomena/visual brightness, HTN, bradycardia.